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Web Annex F. Cost-effectiveness of hepatitis C virus self-testing

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Report: Cost-effectiveness of hepatitis C virus self-testing

Contents

Cost-effectiveness of hepatitis C virus self-testing

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Abstract

Introduction: Hepatitis C virus (HCV) infection is widespread globally. However, less than 26% of the estimated 58 million persons infected knew their diagnosis in 2021. HCV self-testing (HCVST) has been proposed as one approach to promote access to testing and awareness of HCV status. We modelled cost per HCV diagnosis and cure with antibody-testing using HCVST compared to facility-based testing approaches to inform global and national policy towards reaching global 2030 HCV elimination targets.

Methods: We used a decision analysis model with a one-year time horizon to examine the key drivers of cost of diagnosis or cure (in 2019 USD) following introduction of HCVST in four settings: (1) China, men who have sex with men (MSM), HCV antibody prevalence 1%; (2) Georgia, men aged 40–49 years, prevalence 23%; (3) Viet Nam, people who inject drugs (PWID), prevalence 60%; and (4) Kenya, PWID, prevalence 13%. Model parameters such as unit costs, resource use, standard of care testing rates, and linkage to care were informed by data from HCV testing and treatment programs, HIV self-testing (HIVST) programs, and expert opinion. In the base case we assume that a person with a reactive HCVST that links to care would receive a facility-based rapid antibody test (RDT) followed by nucleic acid testing (NAT) to confirm HCV viraemia. We assumed HCVST costs US$5.63 and US$2.25/unit for oral-fluid and blood-based ST respectively, facility-based RDT test cost ranged from US$0.87–US$21.43). Uptake of HCVST increases total testing by 62%, 65% of self-test users link to confirmatory testing, and replacement of facility-based testing by HCVST is 10%. We vary these parameters in sensitivity analyses. We present the economic cost from a provider's perspective reported as incremental cost per patient diagnosed (as by NAT) or cured for HCVST compared to facility-based testing alone in each setting.

Results: Cost per HCV diagnosis under the standard of care (without HCVST) varied by setting from US$35 in Viet Nam to US$361 in Kenya. HCVST increased the number of people tested, diagnosed, and cured, but at higher cost. The cost per diagnosis with self-testing is greater than standard of care, with the incremental cost per diagnosis US$104 in Viet Nam, US$163 in Georgia, US$587 in Kenya, and US$2647 in China, driven by differences in prevalence in each setting. In sensitivity analysis, reducing the cost of oral-fluid based ST or switching to cheaper blood-based ST, increasing uptake of HCVST and linkage to facilities, or going directly to NAT testing, all reduced cost/diagnosis in all settings. Increased cost of ST, high substitution of ST for standard of care tests, low linkage to care and low ST sensitivity increased the cost per diagnosis or cure. The incremental cost per cure was lowest in Georgia (US$1418), with similar outcomes in Viet Nam (US$2033), and Kenya (US$2566), and highest cost in China (US$4956), due to differences in treatment cost. The cost/cure was affected by the same factors as the cost/diagnosis in sensitivity analysis.

Conclusions: The cost per HCV diagnosis or cure for HCVST is higher compared to standard testing in all settings, use of HCVST increased the number of people diagnosed, and therefore linked to care,

treatment, and cure. Introducing HCVST is more cost-effective in populations with high prevalence. The total cost of the increased case-finding is also impacted by the cost of HCV treatment in each setting.

Introduction

The Global Viral Hepatitis Strategy aims to eliminate viral hepatitis (including hepatitis C virus, HCV) as a public health threat by 2030 *(1)*. However, of the estimated 58 million persons infected with HCV in 2021, only 26% knew their diagnosis *(2)*. Self-testing for hepatitis C virus (HCVST) has been proposed as an approach to promote access to testing and awareness of HCV status. Self-testing is a process by which an individual collects his or her own specimen, performs a rapid diagnostic test (RDT), and interprets the result.

Self-testing for HIV (HIVST) has been recommended by the World Health Organization (WHO) as an approach to HIV testing services since 2016 *(3)*. The use of HIVST is now widespread, with 88 countries having policies supporting HIVST, of which nearly half are implementing HIVST routinely as of July 2020 *(4)*.

As countries scale up hepatitis C treatment to reach viral hepatitis elimination targets by 2030, identifying individuals who are not aware of their infection, and unlikely to seek out facility-based testing, will be critical. During the COVID-19 pandemic, healthcare systems have been strained, with healthcare resources diverted to tackle the pandemic, resulting in delays to HCV screening and treatment programs *(5)*. HCVST provides a mechanism to sustain or increase HCV testing rates despite these challenges, with application to the general population as well as key populations expected to have high prevalence of HCV infection, such as people who inject drugs (PWID), and men who have sex with men (MSM).

Although no HCV self-tests are currently on the market, companies that produce RDT for HCV are adapting professional-use tests as self-tests. In addition to determining the usability, feasibility, and accuracy of self-tests, it is important to consider the cost-effectiveness and affordability of introducing self-testing alongside standard testing services. In this study, we use self-test to refer either to an individual conducting the test and interpreting the result by themselves, or to individuals assisted to use the self-test directly by peers or community outreach workers.

It is estimated that around a quarter of those infected with HCV go on to clear their infection spontaneously, so a multi-step testing process is used to confirm active infection (viraemia). The WHO-recommended pathway of testing someone for HCV begins with serological testing with an RDT or laboratory-based immunoassay; those who have a positive (reactive) result are then tested using HCV RNA nucleic acid test (NAT) or core antigen test to confirm viraemia *(6)*. Self-testing can be used as a screening test, followed by additional serological testing at facilities for those with reactive HCVST results followed by a NAT or core antigen test.

Policy makers and healthcare providers will have to decide on whether to implement HCVST, in what populations, and with what testing pathways. In this study, we explore the cost and cost-effectiveness, in terms of cost per diagnosis and cost per cure, of HCVST compared to standard HCV testing pathways alone. The WHO is developing guidance related to HCVST, and the cost-effectiveness analysis presented here will inform this guidance along with a systematic review, recent studies of usability and feasibility *(7)*, and qualitative values and preferences assessments *(8)*.

Methods

In this cost and cost-effectiveness study of HCVST, we focus on four case studies of different populations with varying prevalence of HCV:

- PWID in Viet Nam and Kenya,
- MSM in China,
- men aged 40–49 in Georgia.

The case studies were chosen to represent self-testing in a variety of low and middle-income country contexts, and for different risk groups and prevalence levels. They were selected based on availability of data on HCV testing and treatment costs, HIVST data and/or costs, and/or usability and feasibility/acceptability outcomes for HCV self-testing (HCVST) *(7)*.

The costs of distributing self-tests and of standard of care testing and treatment, and the baseline cascade of care and loss to follow-up at each step differ for each case study. Key details and assumptions are presented in Table 1. Parameter estimates were gathered from literature on HCV testing and treatment programs, HIVST programs, as well as from expert opinion and manufacturers (self-test unit costs).

We explore alternative models and pathways to HCVST, including whether HCVST is offered alongside HIVST (Kenya and China), whether confirmatory NAT testing for viraemic infection is done automatically on samples from those with a reactive facility-based serologic test (reflex testing; Kenya and Viet Nam), and whether self-tests are peer-guided (Kenya and Vietnam). In all settings we allow two separate pathways of linkage from self-testing to facility-based care, that is, whether a reactive self-test leads to the standard pathway of facility-based repeated serologic testing ("repeat serologic testing") or directly to confirmatory NAT testing for viraemic infection ("direct to NAT"). Although core antigen testing is a WHO-recommended option for confirmation of viraemic infection, in this study, we only evaluate pathways using NAT testing as it is the main viraemic infection confirmation method used in all case study settings.

Model structure

We developed a decision-tree model representing the path from HCV testing through to diagnosis, treatment and cure (Figures 1 and 2). The model is based on a cross-sectional evaluation of the proportion of the population of interest who do not know their status, and testing and linkage to care rates that are expected within one year. The population examined differs by case study setting. The model represents three pathways for the study population (Figure 1A):

- standard of care testing, in which people receive facility-based testing and do not get self-tests;
- no testing, for the proportion of the population who remain untested by any method;
- and self-testing, which provides testing for a subset of the group who otherwise would not access testing, as well as replacing some of the standard of care tests with self-tests.

Those in the no-testing pathway are assumed to not be diagnosed or access HCV care in the modelled year. Standard of care testing consists of facility-based anti-HCV antibody testing, with anti-HCV positive individuals receiving confirmatory HCV RNA NAT. Those with confirmed infection are referred for pre-treatment clinical assessment, treated, and then evaluated for sustained virological response using NAT to confirm cure (normally 12 weeks after treatment). Loss to follow-up is accounted for at each step (i.e., not proceeding to the next step in the pathway), based on the cascade of care observed in each setting. Self-testing follows a similar pattern, but self-test results are separated into five outcomes:

1) self-test result conducted but result not reported;
2) reactive self-test result which links directly to confirmatory NAT testing for viraemic infection (direct to NAT scenario);
3) reactive self-test result with retesting with standard of care HCV antibody testing (repeat serologic testing scenario);
4) negative self-test, which is assumed to not lead to follow-up testing; or
5) an invalid test result, such as if the result is not readable by the individual, in which case they would receive repeat serologic testing.

The same model structure is used to represent different self-testing models in each setting, including peer-guided self-testing for PWID in Kenya and Viet Nam, with differences incorporated in the cost and

transition parameters for the relevant case studies. Linkage to care after the self-test is different depending on test result, on the assumption that those with negative self-tests are unlikely to report their result to a health centre, and if they do they will not receive confirmatory testing. The proportion of individuals linking to care/reporting their result after self-testing is incorporated within the transitions from self-testing to the five follow-up arms.

Analysis

For each setting, we compared the introduction of HCVST in terms of numbers of individuals diagnosed or cured, and total cost, cost per diagnosis, and cost per cure, to a counterfactual scenario in which no self-testing occurs. Cost per diagnosis and cost per cure were calculated in terms of the incremental cost effectiveness ratio (ICER). The ICERs were calculated by dividing the difference in cost between the HCVST scenario and the no self-testing scenario (incremental cost) by the difference in the number of people diagnosed/cured between the HCVST scenario and the no self-testing scenario (incremental effect). This provides a measure of the extra cost per extra person diagnosed or cured with the introduction of HCVST. Details of how parameters and costs are incorporated within the model are given in Tables 2 and 3.

Base-case assumptions

We use the repeat serologic-testing pathway as the base case, which assumes that individuals with a reactive self-test that present to a healthcare facility are tested by the standard of care pathway starting from a facility-based serologic test. This facility-based serologic test is assumed to be the SD Bioline HCV rapid test (Abbott Diagnostics, IL, USA) which has an overall sensitivity of 95% (93–96%) and specificity of 100% (99–100%) *(9)*.

In the base case HCVST analysis for each setting, we present the cost-effectiveness of using oral fluid-based self-tests (OraQuick® HCV Rapid Antibody Test, OraSure Technologies, PA, USA), as these were evaluated in the HCVST usability study *(7)*, and oral fluid-based tests were preferred to blood-based tests in HCVST values and preferences studies *(8)*. The sensitivity and specificity of the OraQuick® test are reported to be 98% (95% CI 97–99%) and 100% (95% CI 90–100%), respectively *(10)*. We adjust the sensitivity and specificity to account for misinterpretation of results during self-testing, as observed by inter-reader agreement in the usability studies in each setting *(7)*. In addition, we account for a proportion of self-tests which are used incorrectly, so that no result is able to be reported, but which still lead to the individual linking to facility-based testing (invalid test result); in the base case we assume that 3% of self-test results are invalid. The cost of the oral fluid-based HCVST was estimated to be US$4.50 plus 25% overheads (US$5.63 total), based on expert opinion of the authors, drawing on past experience from HIVST and knowledge of current HCV diagnostic test pricing.

The uptake of self-testing and linkage to care parameters were determined based on randomized controlled trials of HIVST, with 65% of reactive or invalid self-tests linking to facility-based testing, and self-testing leading to a 62% increase in the number of people tested *(11)*. The number of people undertaking self-tests is therefore calculated as a function of the number accessing standard of care testing in each setting, and assuming 10% of people that otherwise would access standard of care, use self-tests instead (substitution) *(12)*. In addition, we assume no difference in treatment initiation or success parameters between the standard of care vs self-testing scenarios, as HIVST trials showed no difference in treatment initiation for those who were self-tested (risk ratio 0.98, 95% CI 0.86–1.11) *(11)*. Setting-based parameter assumptions, such as the standard of care costs, HCV prevalence, and cascades of care, are presented in Table 4.

Sensitivity analysis

In sensitivity analysis we explore the following scenarios:

- **Direct to NAT:** Patients are tested by NAT testing following a reactive self-test;
- **EIA standard of care:** Standard of care antibody testing (including in the no self-testing counterfactual for this scenario) and repeat serologic testing are by enzyme immunoassays (EIA), which are more expensive than RDT and have sensitivity and specificity of 100% as they are the gold standard against which the RDTs are compared;
- **Blood-based HCVST:** Using a blood-based self-test based on the PMC First Response HCV Card Test (Premier Medical Corporation, Mumbai, India), which has an overall sensitivity of 96% (94–97%) and specificity of 99% (99–100%) *(9)*. The professional-use version of this tests costs an average of US$0.90 per the global fund pricing list *(13)*. We assume the self-test cost will be double this cost to account for additional costs of packaging, plus 25% overheads (US$2.25 total);
- **High cost blood-based HCVST:** Use blood-based self-test but assume the total cost is doubled to US$4.50.
- **High cost oral fluid HCVST:** Double the cost of oral fluid-based HCVST to US$11.25 compared to US$5.63 in the base case;
- **Equal cost HCVST:** Set the cost of HCVST including distribution costs to be equal to the standard of care RDT test cost in each setting;
- **Low HCVST performance**: Reduced HCVST performance to 90% sensitivity and 97% specificity from 98% and 100% in the base case, to reflect reduced test performance observed in samples from people co-infected with HIV *(9)*;
- **High inter-reader agreement:** Increase the inter-reader agreement to 100% to reflect improved successful usage of the self-tests;
- **High or low linkage:** Assume 50% or 80% of reactive self-tests link to facility-based testing compared to 65% in the base case. Higher linkage to care is possible particularly in Viet Nam and Kenya where testing is assumed to be peer-led;
- **High or low HCVST uptake:** Increase the uptake of self-testing to reach an 80% increase in overall testing or reduce the uptake of self-testing to reach only a 30% increase in overall testing;
- **High or low substitution:** Vary the proportion of those using self-testing instead of facility-based testing to be 20% or 5% instead of 10% in the base case, while keeping the overall increase in overall testing at 62%.
- **Low or high self-test success:** Vary the proportion of invalid self-test results to be 5% or 1% compared to 3% in the base case.

Costing

We gathered full costing data, accounting for overheads, staff time, training, outreach, facilities, and start-up costs where possible. In two settings (Kenya and China) the cost of HCVST was assumed to be incremental to existing HIVST programs (Table 2), which means that fixed costs, which would be used for HIVST with or without HCVST, were excluded from the costing estimate.

Most cost data were identified in USD from between 2017–2019, with these being adjusted as necessary to present all costs in 2019 USD, by using the consumer price index (CPI) for the study country *(14)*. The CPI value for Kenya was not available for 2019 so was assumed to grow in the same ratio from 2018 as seen from 2017 to 2018. Some cost data from China were received in Chinese Yuan (RMB) [Chen, personal communication; Ong, personal communication], these were assumed to represent prices in 2019 and were converted to USD using the 2019 average exchange rate per USD (6.91 RMB per USD) from the International Monetary Fund's International Financial Statistics.

Results

Cost of standard of care HCV testing without self-testing

In the absence of HCVST, the costs per diagnosis and cure vary by setting due to differences in prevalence, testing costs, and treatment costs. The cost per diagnosis (excluding treatment-related costs) is estimated to be US$35 in Viet Nam, US$55 in Georgia, US$162 in China, and US$361 in Kenya. The cost per cure comes to US$1238 in Georgia, US$1839 in China, US$1943 in Viet Nam, and US$2284 in Kenya. The cost per cure is much more similar across settings than the cost per diagnosis, as the cost of treatment itself is similar across all settings (US$1415–US1543 in Kenya, Viet Nam and China, and approximately half that amount, US$784, in Georgia). On the other hand, the cost of the facility-based RDT test varies 25-fold from US$0.87 in China to US$21.43 in Kenya (Table 4).

The absolute numbers of people diagnosed (Table 5) or cured (Table 6) in one year in the absence of HCVST are dependent on the population size and prevalence in each setting. In China, this is equivalent to 53 diagnosed and 41 cured per 100 000 MSM (antibody prevalence 1.0%); in Viet Nam 18 440 diagnosed and 14 440 cured per 100 000 PWID (antibody prevalence 66.0%); in Georgia 1333 diagnosed and 801 cured per 100 000 men aged 40–49 (antibody prevalence 22.7%); and in Kenya 3353 diagnosed and 2691 cured per 100 000 PWID (antibody prevalence 12.9%).

Cost and impact of HCVST in the base case

In the base case, introducing HCVST increases the number of individuals tested by 62%, which increases the numbers diagnosed and cured by 30.6% in Viet Nam, 34.6% in Kenya, 35.0% in Georgia, and 34.6% in China (Figure 3); the variation is due to slight differences in the cascade of care in each setting (see Table 4).

Tables 5 and 6 show the ICERs for the base-case implementation of HCVST compared to the counterfactual of no HCVST. In addition to increasing the number of individuals diagnosed, introducing HCVST increases the cost per diagnosis in all settings. The ICER per additional person diagnosed with the introduction of HCVST is lowest in Viet Nam (US$104), US$163 in Georgia, US$587 in Kenya, and US$2647 in China (Table 5). The variations in the cost per diagnosis by setting relates to the differences in HCV prevalence in each study setting, with cheaper costs in the settings with higher prevalence. The ICER per person cured ranges from the lowest at US$1418 in Georgia, to US$2030 in Viet Nam, US$2566 in Kenya, and US$4956 in China (Table 6). As with the standard of care scenario, the HCVST cost per cure is driven by the cost of treatment in each setting.

Sensitivity analysis

In the scenarios assessed, uptake of HCVST and linkage to healthcare facilities after self-testing have the largest impact on the number of people diagnosed compared to the base case of HCVST (Figure 4).

In all settings, the cost per diagnosis is sensitive to the cost of HCVST itself (Figure 5). When the HCVST price is the same as the standard of care RDT, the cost per diagnosis is only slightly higher than the no HCVST counterfactual, and much lower than the base-case HCVST scenario in each setting, except for Kenya where standard RDT costs are high. The largest difference in cost compared to the base case in all settings is when the HCVST price is double the base-case scenario.

High substitution of self-tests for standard of care tests, high HCVST uptake, and low linkage also lead to higher cost per diagnosis, while low uptake of HCVST, and using the cheaper blood-based HCVST decrease the total cost per diagnosis.

If the standard of care test were by EIA rather than RDT without HCVST and after introduction of HCVST, the total number of people diagnosed would be slightly higher (due to greater test accuracy), and the cost of standard of care would be much higher (due to higher cost of EIA compared to RDT). In Georgia and Kenya, the total cost per diagnosis would be slightly lower after the introduction of HCVST if EIA testing were the standard of care test. That is because in those settings the cost of the HCVST is much lower than that of EIA (self-test cost including distribution cost comes to 49% of the cost of EIA in Kenya, and 26% in Georgia).

The differences in the ICER per diagnosis and cure under the sensitivity-analysis scenarios are shown in Figures 6 and 7, compared to the base case. Similar patterns are seen across all settings and are related to the factors that impact the total number diagnosed and cost per diagnosis. The ICER per diagnosis increases most when the cost of the HCVST increases; there is low uptake of HCVST; when linkage is low; as well as when there is low performance of the HCVST or high substitution of self-tests for standard of care tests. This pattern holds across all countries, with the EIA as standard of care scenario also having a slightly higher ICER per diagnosis in Georgia and Kenya. Low self-test success (proportion of invalid self-test results of 5%) has little impact in all settings except for Kenya, where it increases the ICER per diagnosis slightly.

Reductions in the ICER are seen with use of the blood-based HCVST, even at double its usual price, when there is high uptake of HCVST, high linkage to facility-based testing, high inter-reader agreement, and low substitution of self-tests for standard of care tests. Going directly to NAT testing after a reactive HCVST result also reduces the ICER in all settings. The largest decrease in the ICER per diagnosis is seen when the HCVST price is matched to the standard of care RDT test cost, with the exception of Kenya where this increases the ICER slightly.

The ICER per cure is impacted by the same factors as the cost per diagnosis. Although the relative magnitudes differ slightly, the pattern is the same as seen in the cost per diagnosis (Figure 7).

Discussion

Our aim in this study was to evaluate the cost-effectiveness of HCVST compared to standard facility-based testing. The introduction of HCVST has the potential to increase the number of people who know their status, are diagnosed with chronic HCV, and successfully treated, as we saw in all settings modelled here. We found that cost per HCV diagnosis under the standard of care (without HCVST) varied widely by setting, from US$35 in Viet Nam to US$361 in Kenya, due to differences in prevalence and test costs. The incremental cost per diagnosis with the addition of HCVST follows the same pattern as the standard of care, with the cost inversely associated with prevalence, ranging from US$104 in Viet Nam to US$2647 in China. Other factors that affect cost per diagnosis include HCVST cost, uptake, substitution of HCVST for standard of care, linkage rate and referral pathway. Differences in the cost per cure were driven primarily by treatment costs rather than the cost of diagnosis.

The ICER of HCVST is impacted strongly by the price of the HCVST itself, and the uptake of the tests, with higher uptake leading to a reduction in the ICER. However, substitution of self-tests for standard of care tests is inversely associated with the ICER, due to the generally higher cost of HCVST compared to the standard of care. Performance (sensitivity and specificity) and usability of the tests in terms of inter-reader agreement had a small impact on the ICER. If reactive HCVST results are referred directly to NAT for confirmation of viraemia without intervening antibody tests, this also decreases the ICER slightly.

Research on HCVST is limited, and implementation research is needed to pilot different models and pathways to care. However, lessons from HIVST can be applied as there are many similarities. For

example, both HIV and HCV are stigmatized, require a multi-step testing process, and in many settings the epidemics are concentrated in different key populations. However, there is a higher proportion of HCV-infected people who do not know their diagnosis compared to HIV. The difference in treatment options, such as the possibility of cure for HCV as opposed to lifelong treatment for HIV, and the relatively wide availability of HIV treatment compared to HCV treatment in some settings, will also inform implementation decisions and acceptability of interventions for focus populations.

This study is the first to estimate the potential cost and impact of HCVST in terms of increasing access to diagnosis and cure, and by necessity we had to make assumptions about many parameters. Where possible, we triangulated sources of information and sought expert opinion in the absence of published literature. A strength of this study is that we used real-world examples from the case study settings, including locally observed costs, HCV prevalence, HCVST feasibility tests, and cascades of care. Where local estimates were not available for HCV, we drew on HIV work in the same populations, including adapting the costs of implementation of HIVST in Kenya and China.

There are several limitations of this study, particularly in uncertainty around parameters regarding uptake of self-testing, and in the lack of information about how HCVST will be implemented. We used data from HIVST where possible, but differences between the diseases could affect the accuracy of predictions. In addition, the four specific case studies may not be broadly generalizable, although they were selected to represent different populations (PWID, MSM, general population), a wide range of HCV prevalence settings, and testing models and pathways within sensitivity analyses. In addition, the study only uses a one-year time horizon, focusing on the outcomes of number of people diagnosed and cured. We do not capture the long-term benefits of diagnosis and curing people of HCV, which will lead to reduced morbidity and mortality from end-stage liver disease, as well as reduced onward transmission. In this preliminary study, it was not feasible to incorporate a model of disease progression and HCV transmission.

In future work on HCVST, presenting outcomes in terms of cost per quality-adjusted life year (QALY) or disability-adjusted life year (DALY) will allow decision makers to compare value for money across different types of interventions. As it stands, the cost per diagnosis and cost per cure of HCVST can be compared to cost per diagnosis and cure of alternative approaches that may be available to increase linkage to care, as well as to the current cost per diagnosis in the absence of HCVST. Our results indicate that the introduction of HCVST will allow for increases in diagnosis and cure of HCV-infected people, although this will require additional resources compared to the current standard of care testing and treatment pathway.

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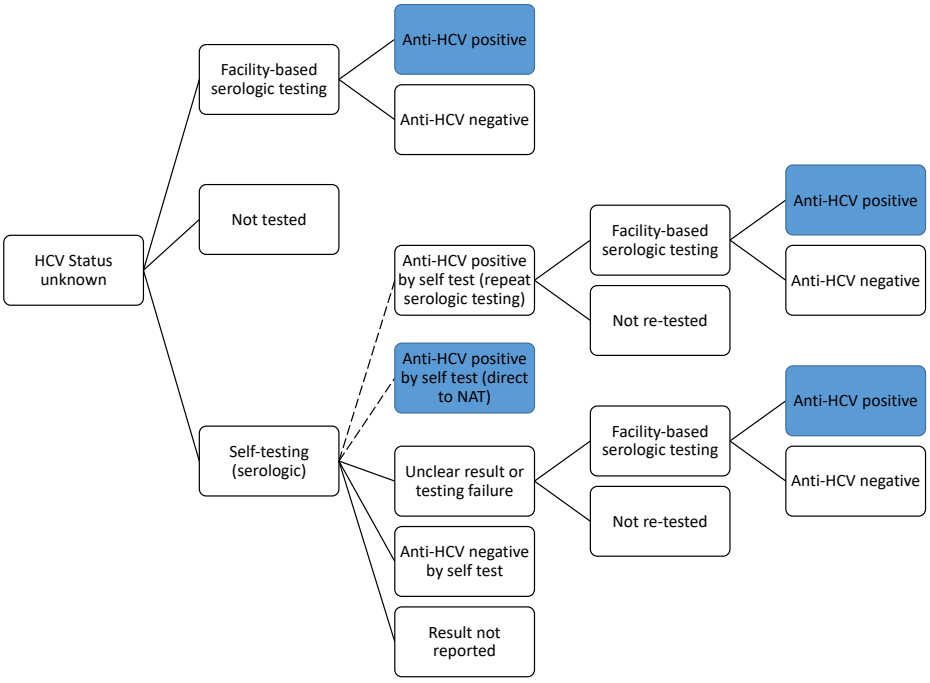
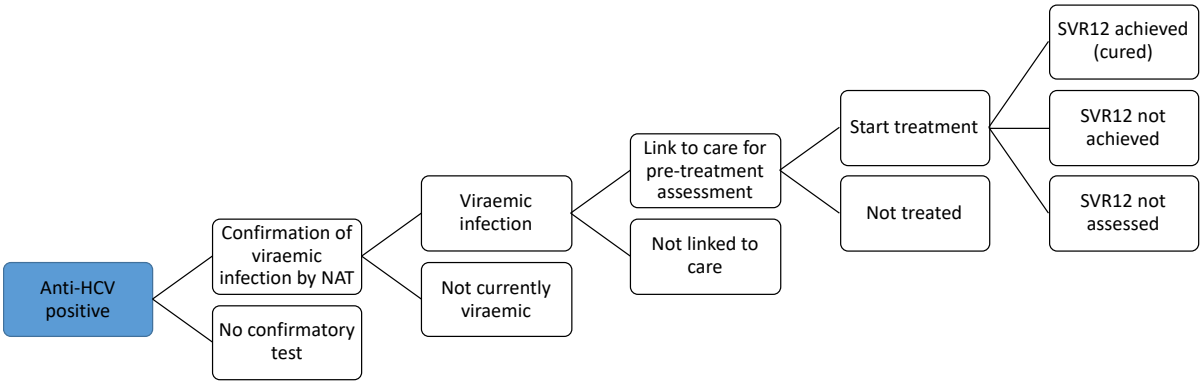
Figures

Figure 1: Flow chart representing scenarios analysed for the introduction of HCVST



Note: Blue boxes represent patients who are anti-HCV positive and link to confirmatory diagnosis (see Figure 2). The dashed lines represent the two possible self-testing scenarios leading to either repeat serologic testing or direct to NAT, which are examined separately.

Figure 2: Flow chart representing pathway of care from receiving a positive HCV antibody test through to treatment and cure



Note: Blue box represents anti-HCV positive individuals from all testing pathways (see Figure 1).

Figure 3: Cascade of care of patients tested, antibody positive, diagnosed viraemic, treated, and cured in each setting for the standard of care with no HCVST compared to the introduction of HCVST (Base-case analysis)

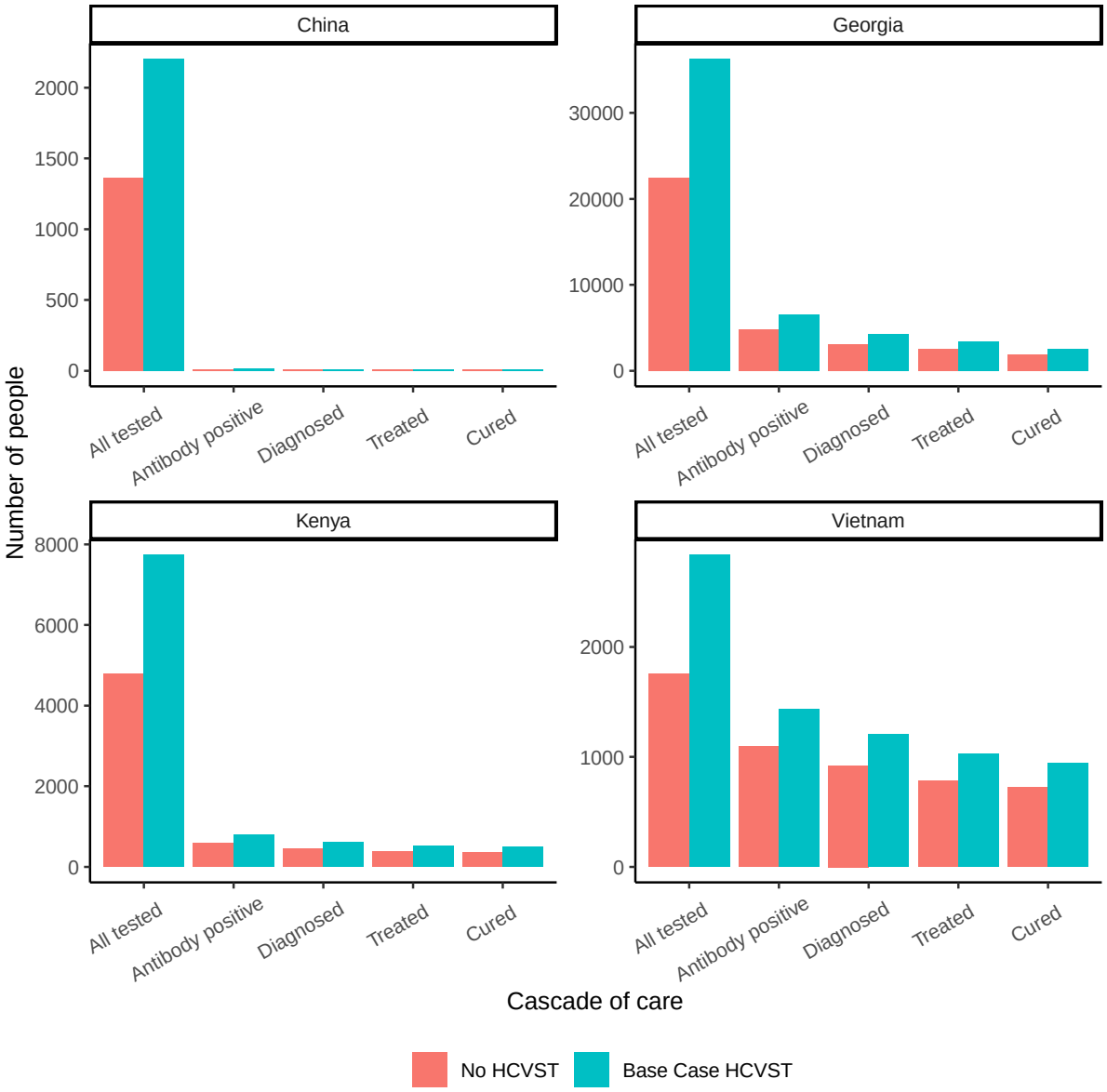
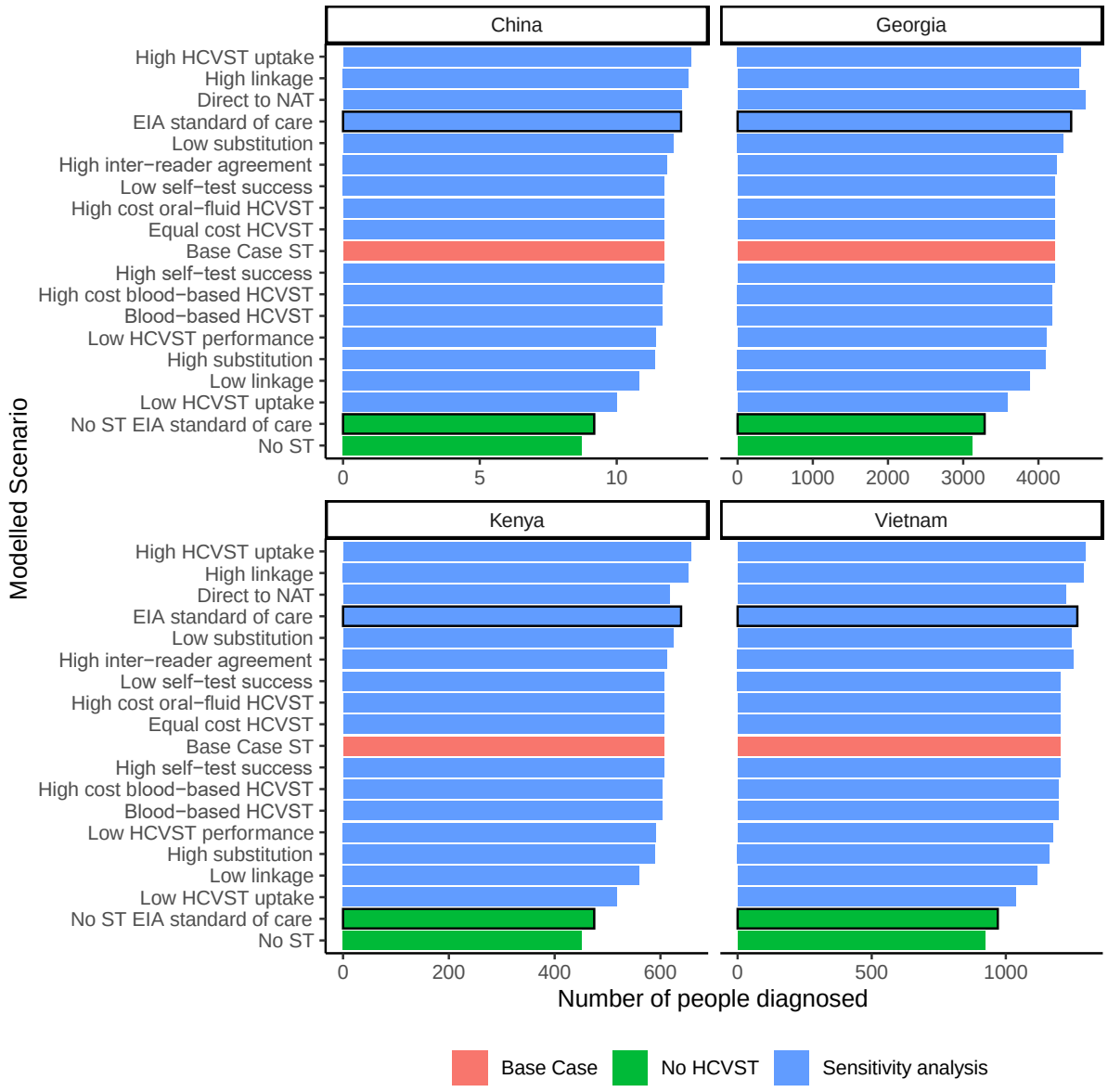
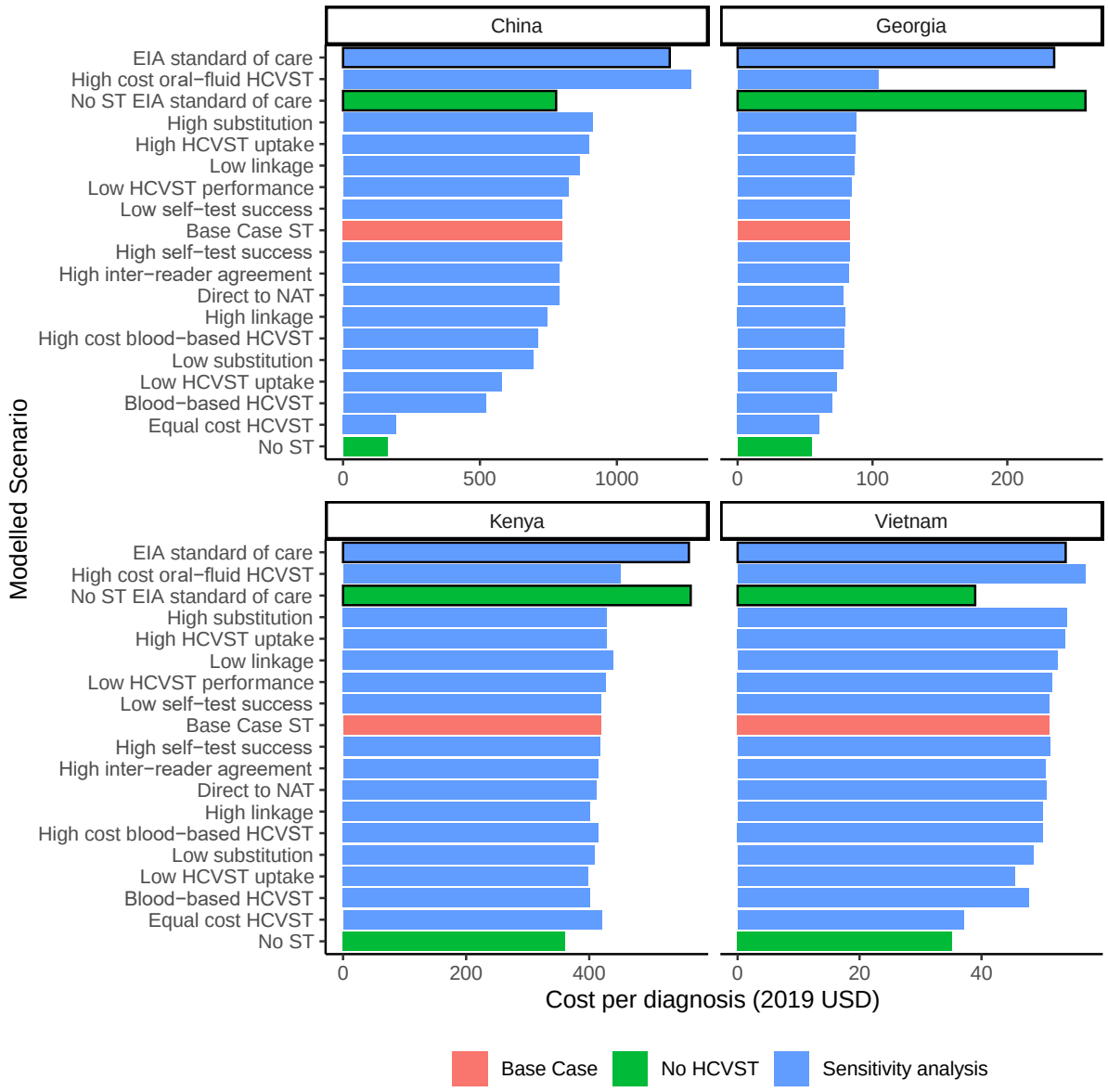


Figure 4: The number of people diagnosed in each setting for each modelled scenario considered in the sensitivity analysis, compared to the counterfactual with no HCVST (in green), and the base case with HCVST (in red)



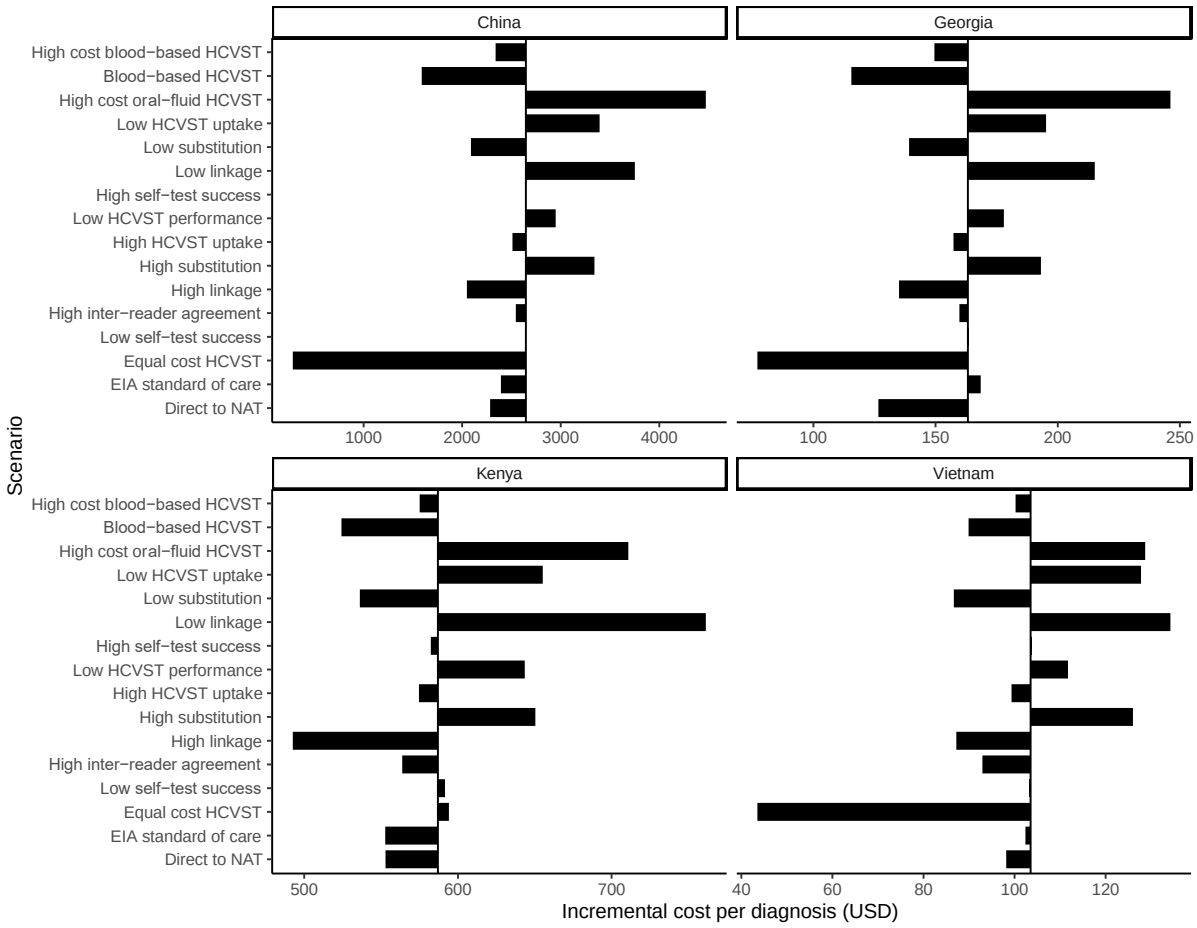
Note: Bars outlined in black indicate the scenarios with and without HCVST in which EIA is the standard of care antibody test.

Figure 5: The cost per patient diagnosed with HCVST (excluding the costs of treatment) in each population, for each modelled sensitivity analysis, compared to the counterfactual with no HCVST (in green), and the base case (in red)



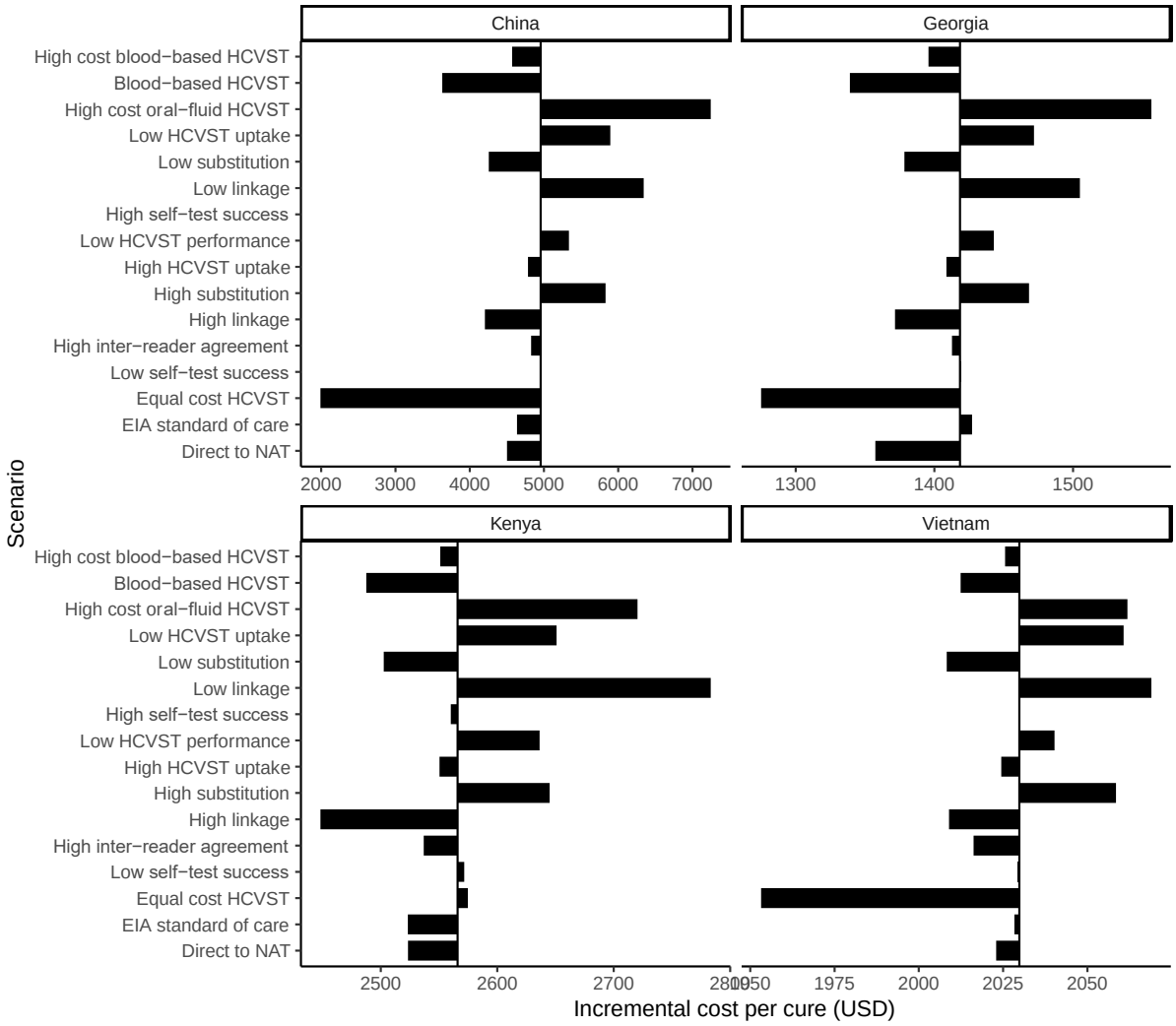
Note: Bars outlined in black indicate the scenarios with and without HCVST in which EIA is the standard of care antibody test.

Figure 6: Tornado plot showing the impact of varying parameters in sensitivity analysis on the incremental cost per diagnosis



Note: The vertical line represents the base-case incremental cost per diagnosis (see Table 5), and the end of each bar represents the incremental cost per diagnosis in each modelled scenario, with the length of the bar representing the magnitude of the difference from the base case. Note that the x-axis scale is different for each country.

Figure 7: Tornado plot showing the impact of varying parameters in sensitivity analysis on the incremental cost per cure



Note: The vertical line represents the base-case incremental cost per cure (see Table 6), and the end of each bar represents the incremental cost per cure in each modelled scenario, with the length of the bar representing the magnitude of the difference from the base case. Note that the x-axis scale is different for each country.

Tables

Table 1: Case study characteristics

Location	**Nairobi, Kenya**	**Georgia**	**Haiphong, Viet Nam**	**Zhuhai, China**
Population	PWID	Men 40–49*	PWID	MSM
Population size	13 450	234 200	5000	17 000
HCV antibody prevalence	13% (11–15%)	23% (18–29%)	66% (46–87%)	1% (0.6–1.5%)
Self-testing (ST) approach	Peer-led testing by outreach workers from harm reduction drop-in centers; demonstration and guidance on test use provided	Assume distribution model in which ST sent through post when requested by target population	Peer-distributed testing by outreach workers from community-based organizations (CBOs)	ST advertised through social media and posted; cost of test reimbursed if result is uploaded
Standard of care	Facility-based HCV testing at a drop-in harm-reduction center	HCV testing widely available including for all inpatients, other target groups	PWID tested as part of respondent-driven sampling surveys	Testing available privately or through CBOs
HCVST integrated within HIVST program	Yes	No	No	Yes
Assume reflex RNA NAT testing after standard antibody test	Yes	No	Yes	No
Key sources	*(7, 15-18)*	*(7, 19-23)*	*(7, 24-27)*	*(7, 28, 29)* Chen, personal communication

*In Georgia, there are high rates of testing coverage already, but middle-aged men represent a large pool of undiagnosed infections. Although men aged 40–49 are estimated to represent 29% of HCV infections in the country, only 6.8% of screening tests have been in this group (Georgia HCV elimination programme data).

Table 2: Transition and cost parameters used in model represented in Figure 1

Step	Transition to step	Cost at step
Initial population	Total population of interest * proportion with unknown status	-
Of initial population:		
Proportion receiving facility-based (FB) serologic testing	Standard testing rate minus proportion that use self-test (ST) instead	Test cost
Proportion receiving ST	New tests plus proportion that switch to using ST instead of standard test	ST cost + distribution
Proportion not tested	1 – standard testing and self-testing	-
Of those with FB serologic test:		
Anti-HCV positive by FB test	Prevalence * (FB sensitivity) + (1-prevalence) * (1 – FB specificity)	-
Anti-HCV negative by FB test	1 – (Prevalence * (FB sensitivity) + (1 – prevalence) * (1 – FB specificity)	-
Of those using self-testing:		
ST result not reported	1 – total next three rows	-
Anti-HCV positive by ST (direct to NAT or standard care pathway)	(prevalence * ST sensitivity * inter-reader agreement + (1 – prevalence) * (1 – ST specificity * inter-reader agreement) * (1 – % test failure) * % link to care if positive	-
Anti-HCV negative by ST	1 – (prevalence*ST sensitivity*inter-reader agreement + (1 – prevalence) * (1 – ST specificity * inter-reader agreement) * (1 – % test failure) * % link to care if negative)	-
Unclear result or ST failure (invalid)	% test failure * % link to care if invalid	-
Of those reporting ST results (repeat serologic testing scenario):		
Retest antibody after invalid anti-HCV ST	% re-tested if link to care	Test cost
Retest antibody (repeat serologic testing scenario) after positive anti-HCV ST	% re-tested if link to care	Test cost
Don't retest antibody after ST	1 – % re-tested antibody	-
Of those receiving FB serologic testing after positive self-test:		
Anti-HCV positive by FB test after positive ST	(Prevalence * ST sensitivity * inter-reader agreement) * FB sensitivity + (1 – Prevalence) * (1 – ST specificity*inter-reader agreement) * (1 – FB specificity) / (Prevalence * (ST sensitivity * inter-reader agreement) + (1 – prevalence) * (1 – ST specificity * inter-reader agreement)	-
Anti-HCV negative by facility-based after positive ST	1 – positive by FB test	-
Of those receiving FB serologic testing after invalid ST:		
Anti-HCV positive by FB serologic test after invalid ST	Prevalence * (FB sensitivity) + (1-prevalence) * (1 – FB specificity)	-
Anti-HCV negative by FB serologic after invalid ST	1 – Prevalence * (FB sensitivity) + (1 – prevalence) * (1 – FB specificity)	-

Note: At each step, the transition parameters leaving a particular cell sum to 1.

Table 3: Transitions and costs from confirmation of viraemic infection onward as shown in Figure 2

Step	Transition to step	Cost at step
Of those anti-HCV positive eligible for NAT testing:		
Confirm infection by NAT after facility-based (FB) test	% receive NAT test	NAT cost
Confirm infection by NAT directly after self-test (ST)	% re-tested if linked to care	NAT cost
No confirmatory test	1 – receive NAT	-
Of those receiving NAT testing:		
Viraemic infection from ST direct to NAT	Viraemic proportion of Ab-positive * (Prevalence * (ST sensitivity * inter-reader agreement) / (Prevalence * (ST sensitivity * inter-reader agreement) + (1-prevalence) * (1 – ST specificity * inter-reader agreement)	-
Viraemic infection by NAT after FB test following ST	Viraemic proportion of Ab-positive * (Prevalence * ST sensitivity * inter-reader agreement) * FB sensitivity / (Prevalence * ST sensitivity * inter-reader agreement) * FB sensitivity + (1 – Prevalence) * (1 – ST specificity * inter-reader agreement) * (1 – FB specificity)	-
Viraemic infection by NAT after FB test only	Viraemic proportion of Ab-positive * (Prevalence * (FB sensitivity) / (Prevalence * (FB sensitivity) + (1 – prevalence) * (1 – FB specificity)	-
Not currently viraemic	1 – positive NAT test	
Of those with chronic infection:		
Link to care for pre-treatment assessment	Link to care (observed care cascade)	Pre-treatment costs
Not linked to care	1 – link to care	-
Of those linked to care:		
Start treatment	Treated (observed care cascade)	Treat cost
Not treated	1 – treated	-
Of those treated:		
Sustained virologic response (SVR)12 achieved	% tested for SVR * % cure	NAT cost
SVR12 not achieved	% tested for SVR * (1- % cure)	NAT cost
SVR12 not assessed	Not tested for SVR	-

Table 4: Parameters used in analysis

Parameter	Kenya	Georgia	Vietnam	China	Source*
Transition parameters					
Population size	13 450	234 200	5000	17 000	*(18, 22, 27, 29)*
Antibody prevalence	12.9%	22.7%	66.0%	1.0%	*(15, 20, 25, 26, 28)*
Unknown HCV status	71.0%	76.0%	70.0%	80.0%	*(15, 21)**
Chronic hepatitis C prevalence among those Ab+	77.0%	80.0%	84.0%	75.0%	*(17, 21, 26)**
Standard of care test uptake among unknown status per year	50.0%	13.0%	50.0%	10.0%	*(21, 26, 29)**
Uptake of self-tests (ST) among otherwise untested (to achieve 62% increase in testing)	31.0%	7.8%	31.0%	6.2%	*(11)*
Percent of facility-based (FB) tests that are replaced with self-tests	10.0%				Assumption
SD Bioline sensitivity	95.0%				*(9)*
SD Bioline specificity	100%				*(9)*
OraQuick sensitivity	98.0%				*(10)*
OraQuick specificity	100%				*(10)*
Test failure rate (invalid result)	3.0%				Assumption
Inter-reader agreement	97.0%	98.0%	88.0%	97.0%	*(7)*
Link to care with positive ST	65.0%				*(11)*
Link to care with negative ST	5.0%				Assumption
Link to care with invalid ST	65.0%				*(11)*
Receive FB test if link to care with positive or invalid ST	100%				Assumption
Receive follow-up test in clinic if report negative ST result	0%				Assumption
Receive NAT test after FB serologic test (assume reflex testing in Kenya and Vietnam)	100%	81.0%	100%	90.0%	*(17, 21)*
Link to care if NAT positive	92.0%	90.0%	89.0%	90.0%	*(15, 26)**
Start treatment if linked to care	92.0%	90.0%	96.0%	90.0%	*(15, 26)**
Cured if start treatment	95.0%	74.0%	92.0%	98.0%	*(17, 21, 26)**
Not tested for SVR	0%	25.0%	5.0%	0%	*(17, 21, 26)**
Cost parameters (2019 USD)					
ST unit cost (oral fluid-based)	5.63				Assumption
ST unit cost (blood-based)	2.25				Assumption *(13)*
Cost of distributing ST	15.46	3.00	10.00	2.52	*(16, 29)*
FB EIA test cost [For Kenya and Vietnam assume double RDT cost]	42.87	32.76	4.44	5.07	*(17, 23, 26)*
FB RDT cost	21.43	2.79	2.22	0.87	
NAT test cost	103.56	27.82	26.00	20.26	

Pre-treatment costs – blood tests, liver disease staging, etc. [For Viet Nam and China calculate as 10% of total treatment costs]	123.29	40.89	171.40	157.00	*(17, 19)*
Treatment costs	1501.49	784.37	1542.60	1414.64	*(17, 19, 24)*

Sources marked with * represent programme data re-analysed for this study.

Table 5: Incremental cost per diagnosis of implementing HCVST (base-case analysis)

Setting	Scenario	Total cost (US$)	Total diagnosed	Incremental cost	Incremental diagnosed	Incremental cost per diagnosis (ICER)
Kenya	No HCVST	$162,685	451	-	-	-
	Base case HCVST	$254,194	607	$91,509	156	$587
Georgia	No HCVST	$171,037	3123	-	-	-
	Base case HCVST	$349,430	4216	$178,393	1,093	$163
Viet Nam	No HCVST	$32,413	922	-	-	-
	Base case HCVST	$61,566	1203	$29,152	282	$104
China	No HCVST	$1416	9	-	-	-
	Base case HCVST	$9393	12	$7977	3	$2647

Note: Cost per diagnosis excludes treatment costs.

Table 6: Incremental cost per cure of implementing HCVST (base-case analysis)

Setting	Scenario	Total cost	Total cured	Incremental cost	Incremental cured	Incremental cost per cure (ICER)
Kenya	No HCVST	$826,740	362	-	-	-
	Base case HCVST	$1,147,729	487	$320,989	125	$2566
Georgia	No HCVST	$2,322,642	1876	-	-	-
	Base case HCVST	$3,254,115	2533	$931,473	657	$1418
Viet Nam	No HCVST	$1,402,615	722	-	-	-
	Base case HCVST	$1,850,412	943	$447,797	221	$2030
China	No HCVST	$12,785	7	-	-	-
	Base case HCVST	$26,690	9	$11,905	2.4	$4956

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